UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

JR

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/894,356	08/18/97	ASHIKARI T	001560-308

HM22/0212

RONALD L GRUDZIECKI
BURNS DOANE SWECKER & MATHIS
P O BOX 1404
ALEXANDRIA VA 22313-1404

EXAMINER	
ZAGHMOUT, O	
ART UNIT	**PAPER NUMBER**
1649	13

DATE MAILED: 02/12/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/894,356	Applicant(s) Ashikari et al
	Examiner Ousama Zaghmout	Group Art Unit 1649

☒ Responsive to communication(s) filed on *Aug 18, 1997*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-27* is/are pending in the application.

Of the above, claim(s) *13-19 and 21* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12, 20, and 22-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4 and 6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Detailed Action

Claims 1-27 are pending.

Claims 1-12, 20, 22-27 were elected by the Applicants with traverse in the restriction requirements response which was filed 10/22/98. Claims 13-19, 21 are withdrawn from further consideration. As claim 24 is present in elected and no-elected inventions, it will be examined on the merit to the extent that it reads in the elected invention.

Applicant's election with traverse of in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the restriction was improperly drafted. This application is a 371 type and as such the PCT rule should have been applied. In addition Applicant contends that the Examiner has failed to explain why the claims in Groups I-III lack unity of invention. On the onset, the Examiner agrees that inadvertently the restriction requirements was drafted as applied in the US practice. However, the bases for the restriction requirement are still deemed valid. The inventions listed as groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Since the gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity is known in the art as evidenced by the Ishizaki et al (FEBS Lett 1988 Oct 10;238(2):424-430) reference, it does not constitute a special technical feature as defined by PCT Rule 13.2. Groups I-III are

directed to gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity. They are further directed to protein and method of acylating a pigment. However, since claim 1 lacks novelty, unity of invention is lacking, because gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity was reported previously by Ishizaki et al (FEBS Lett 1988 Oct 10;238(2):424-430). The cited evidence proves that the technical feature of group 1, gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity, does not make a contribution over the prior art. The claims are not so linked by a special technical feature within the meaning of the PCT Rule 13.2 so as to form a single inventive concept, accordingly, the unity of invention is lacking among all groups. Therefore, The restriction requirement is still deemed proper and is therefore made FINAL.

The CRF submitted was technically bad. As such, it was not entered the database. Please see attached for compliance with sequence requirements.

In the amendment of the claims, please indicate the line number in the claim itself in which the amendment needed to be made (e.g., In claim 14, line 2, page 75). Your help in the aspect is greatly appreciated.

Claim 24 is objected for depending on non-elected claims.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Ist Paragraph

Claims 1-8 and dependent claims 9-12, 20, 22-27 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The claims are generically drawn to a gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity. The specification fails to describe adequate representative species of the claimed nucleic acids by their relevant identifying characteristics, e.g. by sequence or other structure or properties.

Only specific sequences are disclosed. At the time the application was filed, one of skill in the art could not have predicted the relevant identifying characteristics of the nucleic acids of a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity based only on the sequence of the corresponding gene, or a gene encoding any of the amino acid sequences of SEQ ID Nos: 1-6, or a modified amino acid sequence in which amino acid sequences is modified by addition or removal of one or more amino acids, or a substitution with other amino acid(s), or a gene encoding a protein which has the amino acid sequence having a homology of at least 15% or 30% or higher with any of the amino acid sequences of SEQ ID Nos: 1-6, and which has aromatic acyl group transfer activity. Accordingly, one of skill in the art would not have recognized the applicant to have been in possession of the claimed nucleic acids at the time the application was filed. Furthermore, there is no information in the literature or in the specification to predict if nucleotide sequences within this genus are very similar in structural and physical characteristics to define the claimed genus. In addition, it is not clear if these claimed but not disclosed nucleic acid molecules will be able provide a protein with biological activity and desirable traits when expressed in a cell. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that a patent specification contain a written

description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

The separateness of the two requirements has been emphasized in the biotechnology area by two cases. Both cases involved interferences in which the count in question related to a strand of DNA. In one case Fiers v. Sugano [25 USPQ2d 1601 (Fed. Cir. 1993], :"An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself." In the Fiers case, convention priority was denied to a claim to a DNA sequence coding for a specified protein because of the absence of the actual sequence of the DNA in the priority documents. A similar situation occurred in Fiddes v.Baird [30 USPQ2d 1481 (Bd. of Appeals 1993).] where the Board of Appeals stated that "knowledge of amino acid sequence of a protein coupled with the established relationship in the genetic code between a nucleic acid and a protein it encodes would not establish possession of a gene encoding that protein."

Claims 1-12, 20, 22-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabled for isolation of the nucleotide sequence identified in SEQ ID NOs: 1-6 which contains nucleotide sequences that encode a protein having aromatic acyl group transfer activity, and for the construction and introduction of the acyltransferase gene into petunia, does not reasonably comply with the description of the invention requirements regarding the nucleotide sequences of all claimed genes encoding all proteins which are having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity, and with the enablement for the production of transgenic plants with any of these claimed nucleotide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the claims are not commensurate in scope with the enabling support provided. Applicants broadly claim a gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity. Furthermore, applicants claim a gene encoding any of the amino acid sequences of SEQ ID Nos: 1-6, or a modified amino acid sequence in which amino acid sequences is modified by addition or removal of one or more amino acids, or a substitution with other amino acid(s), or a gene encoding a protein which has the amino acid sequence having a homology of at least 15% or 30% or higher with any of the amino acid sequences of SEQ ID Nos: 1-6, and which has aromatic acyl group transfer activity. However, in the instant disclosure, applicants provide and explicitly demonstrate the isolation of the nucleotide sequences identified in SEQ ID NOs:

1-6 which contain nucleotide sequences that encode a a protein having aromatic acyl group transfer activity, and for the construction and introduction of the acyltransferase gene into petunia.

The identification of these sequence and testing them in transgenic plants to determine if they will have any aromatic acyl group transfer enzymatic activity is very critical for the enablement of the claimed invention. This is very critical in the fact that many of these nucleotide sequences including derivatives or homologous sequences need to be present in order to comply with the description requirement. Applicants there is a need to test if any of these claimed gene would indeed have any aromatic acyl group transfer activity. As such, the expression of the claimed DNA molecules in transgenic cells and plants by the applicants is very critical for the enablement of the claimed invention in the light of the fact that the process of transforming plants with individual genes to obtain desired phenotypes is unpredictable. Napoli et al. observed a reversible inhibition of expression of the desired gene, when introduced in sense orientation into a plant, so that the desired phenotype was not observed (The Plant Cell. 1989. Vol. 2: 278-289. see page 279, Abstract). This unpredictability problem is further exemplified recently by the teaching of Boase et al (In Vitro Cell. Dev. Biol.--Plant 34:46–51, January-March 1998)). Boase et al teach a genetic transformation method using Agrobacterium tumefaciens strain LBA4404 and based on the neomycin phosphotransferase II (nptII) selectable marker gene is described for a cultivar of florists' chrysanthemum, Dendranthema Xgrandiflorum 'Peach Margaret'. Boase et al teach the use of flavonoid regulatory cDNA, Leaf color (Lc) from the monocot Zea mays (maize),

under control of the cauliflower mosaic virus 35S promoter, to test if it would serve as a visible, nondestructive pigmentation reporter of transformation in chrysanthemum and to see if it will modify floral and leaf pigmentation. Stable integration of the maize Lc cDNA in `Peach Margaret' was confirmed by Southern DNA analysis. However, no Lc RNA transcripts were detected and no increase in pigmentation was observed in the transformants. In contrast, activity of the nptII transgene in the transformants was confirmed by production of roots in the presence of 20 mg/l kanamycin and challenging leaf explants to regenerate shoots in the presence of 25 mg/l kanamycin (Abstract).

Furthermore, it is important to show traits encoded by the transgenes will be maintained in these transgenic cells and plants when they are used in breeding programs. This is important in the light of the fact that traits encoded by some transgenes have been shown to decline/or disappear at a later stage thereafter. Carvalho et al. teach that expression of a transgenic glucanase was silenced in a homozygous transgenic tobacco line (T17). Carvalho et al. further teach that transgenic glucanase mRNA was detected at high level in the homozygous plant during the first 4 weeks of development. Carvalho et al. further teach that after 4 weeks, the mRNA level decreased gradually. In some Nicotiana sylvestris plants transformed with a p35S-chitinase gene the lower leaves showed a high chitinase content, whereas the upper leaves, formed later in development, showed low chitinase content and co-suppression of both the transgenic and the endogenous chitinase gene (Carvalho et al. The EMBO Journal. 1992. Vol. 11: 2595-2602. The 4th paragraph under the Discussion section).

Applicants failed to address many of these important issues which are essentail for the enablement of the claimed invention. Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth. Thus it is not readily predictable that the genetic modification specifically disclosed will work with other genes or other plants. Applicant has provided no specific guidance as to how to select genes which will give the desired effect or provided guidance with regard to selection of other plants and/or the technique to be used in the modification of these genetic modification of these plants. One wishing to practice the invention is left to proceed through trial-and-error to see what will work and what will not.

In view of the breadth of the claims, unpredictability, lack of guidance in the specification of the results as stated above, it is the examiner's position that one skilled in the art to which it pertains, or with which it is most nearly connected, could not practice the invention commensurate in scope with these claims without undue experimentations.

2nd Paragraph

Claims 1, 4, 6, 7, 8, 25 and dependent claims 2-3, 5, 9--12, 20, 22-24, 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 2-12, 20, 22-27 are rejected for the use of the word " derivative" which render these claims vague and indefinite for particularly failing to point

out and distinctly claim the nucleotide sequence which encoded by these derivatives. This word is not defined precisely and clearly in the claim and the specification does not provide a standard for ascertaining the requisite of amino acid or nucleotide sequences encompassed by the word derivative, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 4 is rejected for the use of the word " modified" which renders the claim vague and indefinite for particularly failing to point out and distinctly claim of these nucleotide sequences will be modified, and if one base of amino acid will be chosen over the other s during the suggested modification process. This word is not defined in the claim and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 4 is rejected for the use of the word " addition or removal of one or more amino acids" which renders this claim vague and indefinite for particularly failing to point out and distinctly claim which amino acid will be added or removed. The specification fails to disclose the basis that one skilled in the art will depend on for the addition or the removal of each one of these claimed amino acids. These words are not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 4 is rejected for the use of the word " substitution" which renders this claim vague and indefinite for particularly failing to point out and distinctly claim which base or amino acid will or will not be substituted. The specification fails to disclose the basis that one skilled in the art will depend on for the substitution of each one of these claimed bases amino acids. This word is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree of substitution, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 6 is rejected for the recitation of " with part " which renders this claim and vague and indefinite for particularly failing to point out and distinctly claim the nucleotide sequence is encompassed by the claimed part. It is not clear if that claimed part is comprising of one base or one amino acid or larger than that. The specification failed to define that claimed part clearly and precisely. Furthermore, the specification does not provide a standard for ascertaining the requisite sequence encompassed in that part, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 7 and 25 are rejected for the use of the word " having" which renders this claim indefinite for particularly failing to point out and distinctly claim the precise and the clear meaning of the word "having". it is not clear if the word "having" means comprising, comprising of, or any other similar meaning. In the absence of an express definition of the word "having" from the specification, the word "having" would appear to be open ended.

Claims 7-8 are vague and indefinite for the recitation of "homology of at least 15% or higher", "homology of at least 30% or higher". However, "homology" or sequence similarity can be calculated by a variety of different methods, whereby the calculated homology between two sequences will be quite different depending on the algorithm used for calculation. Furthermore, the calculation of "homology" is affected by variables such as the relative weight given to the sequence gaps versus mismatches, or whether conservative substitutions are weighted differently from non-conservative substitutions. Since no art-recognized convention exists regarding the calculation of percent homology, the recitation of "homology of at least 15% or higher", and "homology of at least 30% or higher" is vague and indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

a person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ishizaki et al (FEBS Lett 1988 Oct 10;238(2):424-430).

Claims are directed to a gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity. Furthermore, applicants claim a gene encoding any of the amino acid sequences of SEQ ID Nos: 1-6, or a modified amino acid sequence in which amino acid sequences is modified by addition or removal of one or more amino acids, or a substitution with other amino acid(s), or a gene encoding a protein which has the amino acid sequence having a homology of at least 15% or 30% or higher with any of the amino acid sequences of SEQ ID Nos: 1-6, and which has aromatic acyl group transfer activity.

The claimed inventions read on Ishizaki et al as follows:

Ishizaki et al teach cloning and nucleotide sequence of cDNA for the plastid glycerol-3-phosphate acyltransferase from squash. Ishizaki et al teach that partial amino acid sequence and amino acid composition of acyl-(acyl-carrier-protein):glycerol-3-phosphate acyltransferase purified from squash cotyledons were determined. cDNAs encoding this enzyme were isolated from lambda gt 11 cDNA libraries made from poly(a)+ RNA of squash cotyledons by immunological selection and cross-hybridization. One of the resultant clones

contained a cDNA insert of 1426 base pairs and an open reading frame of 1188 base pairs. The amino acid sequence deduced from the nucleotide sequence matched the partial amino acid sequence determined for the enzyme. The results suggest that a precursor protein of 396 amino acid residues is processed to the mature enzyme of 368 amino acid residues, losing a leader peptide of 28 amino acid residues. Relative molecular masses of the precursor and mature proteins were calculated to be 43,838 and 40,929 Da, respectively (See also: PMID: 2458971, UI: 89005726). Each element of the claims is disclosed by the reference. Claims 4-8 were included in the rejection for the use of the words "modified, deletion, addition, substitution, homology" which will make the nucleotide sequence of the reference to read on the claimed invention in these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 20, 22-27 are rejected under 35 U.S.C 103 (a) as being unpatentable over Ishizaki et al (FEBS Lett 1988 Oct 10;238(2):424-430) in view of Heidmann et al

(Nature. 1987. Vol. 330:677-678), Matern et al (Arch. Bioch. Biophys. 1981. Vol.208:233) and Kamsteeg et al (Biochem. Physiol. Pflanzen. 1980. Vol. 175: 403).

These claims are directed to a gene encoding a protein having aromatic acyl group transfer activity or a derivative thereof having said enzymatic activity. Furthermore, applicants claim a gene encoding any of the amino acid sequences of SEQ ID Nos: 1-6, or a modified amino acid sequence in which amino acid sequences is modified by addition or removal of one or more amino acids, or a substitution with other amino acid(s), or a gene encoding a protein which has the amino acid sequence having a homology of at least 15% or 30% or higher with any of the amino acid sequences of SEQ ID Nos: 1-6, and which has aromatic acyl group transfer activity.

Ishizaki et al teach cloning and nucleotide sequence of cDNA for the plastid glycerol-3-phosphate acyltransferase from squash. Ishizaki et al teach that partial amino acid sequence and amino acid composition of acyl-(acyl-carrier-protein):glycerol-3-phosphate acyltransferase purified from squash cotyledons were determined. cDNAs encoding this enzyme were isolated from lambda gt 11 cDNA libraries made from poly(a)+ RNA of squash cotyledons by immunological selection and cross-hybridization. One of the resultant clones contained a cDNA insert of 1426 base pairs and an open reading frame of 1188 base pairs. The amino acid sequence deduced from the nucleotide sequence matched the partial amino acid sequence determined for the enzyme (abstract. See also materials and methods).

Ishizaki et al do not teach or expressly disclose the expression of the isolated gene in transgenic plants.

Heidmann et al thatPetunia hybrida is one of the classical subjects of investigation in plants in which the pathway of anthocyanin biosynthesis has been analysed genetically and biochemically. In petunia cyanidin- and delphinidin-derivatives, but no pelargonidin-derivatives are produced as pigments. This is due to the substrate specificity of the dihydroflavonol 4-reductase of petunia, which cannot reduce dihydrokaempferol. The petunia mutant RL01, which accumulates dihydrokaempferol, shows no flower pigmentation. RL01 served as a recipient for the transfer of the A1 gene of Zea mays encoding dihydroquercetin 4-reductase, which can reduce dihydrokaempferol and thereby provided the intermediate for pelargonidin biosynthesis. Transformation of RL01 with a vector p35A1, containing the A1-complementary DNA behind the 35S promotor leads to red flowers of the pelargonidin-type. Thus a new flower pigmentation pathway has been established in these plants (lines 5-16, page 677).

Matern et al teach the importance of transferases which transfer acyl groups to anthocyanin pigments (see abstract and introduction).

Kamsteeg et al teach the importance of acyl transfer reaction (abstract).

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to use the transformation system taught by Heidmann et al to express the gene taught by Ishizaki et al to produce transgenic plants to produce plants of various flower colors and of great commercial value. The teachings of Matern et al and Kamtseeg et al are of great value in terms of teaching the importance of aromatic proteins with acytltransferase activity in modulation of pigments such anthocyanin. Therefore, the motivation for doing so would have been to produce flower of desirable colors for commercial purposes.

Ishizaki et al, Heidmann et al et al, Matern et al, and Kamsteeg et al, are combinable because they are from a similar problem solving area, viz., manipulation of flower color.

Therefore, it would have been obvious to combine Ishizaki et al, Heidmann et al et al, Matern et al, and Kamsteeg et al to obtain the genetically modified plants as specified in claims 1-12, 20, 22-27. The use of nucleotide sequences of a protein having aromatic acyltransferase activity with various derivatives, addition, substitution and other modification is a matter of choice unless the proof of criticality is provided. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in absence of evidence to the contrary.

Conclusion

No claims are allowed.

Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, L. Smith, can be reached on (703) 308-3909. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M-Faiz Zaghmout Ph.D.

February 4, 1999

L. F. Smith

LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP 1800